J. Am. Chem. Soc. **1993**, *115*, 10992–10993

Theory of Gas-Phase and Solution Stereoselectivities of Hydride Reductions of Cyclohexanone Derivatives by Silicon Hydrides

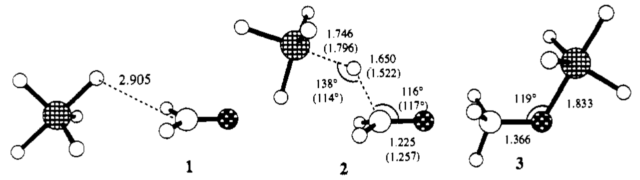
Yundong Wu* and K. N. Houk*

Department of Chemistry, The Hong Kong
University of Science and Technology
Clear Water Bay, Kowloon, Hong Kong
Department of Chemistry and Biochemistry
University of California, Los Angeles
Los Angeles, California 90024

Received March 4, 1993

The origin of stereoselectivity of nucleophilic additions to cyclohexanone derivatives continues to attract lively discussion.[1,2] The clarity of the message of previous theoretical studies is clouded by the exclusion of solvent. A recent report by Squires *et al.* on the stereoselectivity of the gas-phase hydride reductions of cyclohexanones by pentacoordinated alkoxysiliconate ions $RSiH_3(OR')^-$ provides an opportunity to compare directly the experimental results with gas-phase theoretical calculations.[3] We report a theoretical study of the stereoselectivity of hydride reduction of cyclohexanone analogs by SiH_5^-, both in the gas phase and in solution. We predict a dramatic reversal of stereoselectivity of reduction of 1,3-dioxan-5-one from the gas phase to solution and provide new evidence for the role of torsional and electrostatic effects on stereoselectivities.[4–6]

The reaction of SiH_5^- with formaldehyde was studied first.[7] The reaction complex, transition structure, and product were optimized with the 6-31++G** basis set, and energies were calculated at the MP3/6-31++G** level.[8] The results are shown in Figure 1.[9] The reactants form a weakly bound ion–molecule complex. The transition structure is similar to those of hydride transfer reactions.[10,11] The SiH_4 unit it tilted away from the carbonyl oxygen, which minimizes repulsions between the main sites of negative charge. The calculated activation energy is only 0.2 kcal/mol. The formation of separated CH_3O^- and SiH_4 products is exothermic by about 23 kcal/mol. The final product, $CH_3O\text{–}SiH_4^-$ (**3**), is much more stable than the free methoxide plus SiH_4, but there is no O–Si interaction in the transition state.



	1	2	3
6-31++G**	-8.5	-1.1	-45.1 (-17.3)
MP2/6-31++G**	-9.8	-12.1	-55.9 (-24.9)
MP3/6-31++G**	-9.9	-9.7	-55.2 (-23.1)

Figure 1. 6-31++G** structures of the ion–molecule complex **1** of SiH_5^- and formaldehyde, transition structure **2**, and the final product of the gas-phase reaction of SiH_5^- with formaldehyde. The relative energies (kcal/mol) are corrected with zero-point energies. The 3-21G geometrical parameters of **2** are given in parentheses. The relative energy of CH_3O^- plus SiH_4 is shown in parentheses.

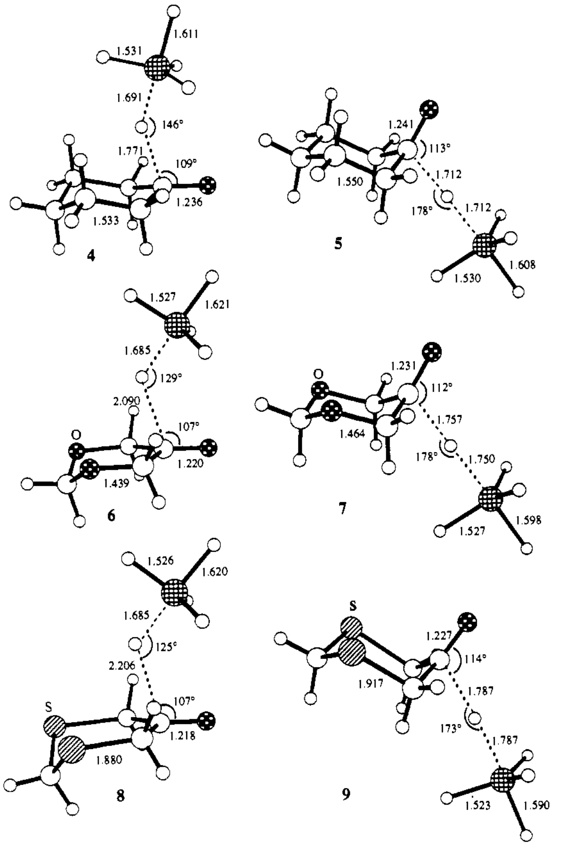


Figure 2. 3-21G axial and equatorial transition structures for the reaction of SiH_5^- with cyclohexanone (**4** and **5**), 1,3-dioxan-5-one (**6** and **7**), and 1,3-dithian-5-one (**8** and **9**).

The transition structures for the reactions of SiH_5^- with cyclohexanone, 1,3-dioxan-5-one, and 1,3-dithian-5-one were located with the 3-21G basis set. The results are shown in Figure 2. No higher level optimization was attempted, because the calculations for **2** using the 3-21G basis set give a structure similar to that obtained with the 6-31++G** basis set. The energies were evaluated with the MP2/6-31G* calculations with an added set of s and p orbitals on the H atoms of SiH_5^-. Solvent effects were modeled with the SCRF method[12] with methanol as solvent ($\epsilon = 32.6$). The calculated energies of the transition structures

---

(1) For recent leading references, see: (a) Wu, Y. D.; Houk, K. N.; Paddon-Row, M. N. *Angew. Chem., Int. Engl.* **1992**, *31*, 1019. (b) Paddon-Row, M. N.; Wu, Y. D.; Houk, K. N. *J. Am. Chem. Soc.* **1992**, *114*, 10638. (c) Frenking, G.; Köhler, K. F.; Reetz, M. T. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1146.

(2) (a) Cieplak, A. S. *J. Am. Chem. Soc.* **1981**, *103*, 4540. (b) Cieplak, A. S.; Tait, B. D.; Johnson, C. R. *Ibid.* **1989**, *111*, 8447. (c) Hahn, J. M.; le Noble, W. J. *J. Am. Chem. Soc.* **1992**, *114*, 1916 and references there in. (d) Mehta, G.; Praveen, M. *Tetrahedron. Lett.* **1992**, *33*, 1759 and references therein. (e) Kumar, V. A.; Venkatesan, K.; Ganguly, B.; Khan, F. A.; Mehta, G. *Ibid.* **1992**, *114*, 3069.

(3) Ho, Y.; Squires, R. R. *J. Am. Chem. Soc.* **1992**, *114*, 10961.

(4) (a) Cherest, M.; Felkin, H. *Tetrahedron Lett.* **1968**, 2201; 2205. (b) Anh, N. T. *Fortschr. Chem. Forsch.* **1980**, *88*, 145.

(5) (a) Wong, S. S.; Paddon-Row, M. N. *J. Chem. Soc., Chem. Commun.* **1990**, 456; (b) *Aust. J. Chem.* **1991**, *44*, 765; (c) *J. Chem. Soc., Chem. Commun.* **1991**, 327.

(6) (a) Wu, Y.-D.; Tucker, J. A.; Houk, K. N. *J. Am. Chem. Soc.* **1991**, *113*, 5018. (b) Wu, Y.-D.; Houk, K. N. *J. Am. Chem. Soc.* **1987**, *109*, 908. (c) Houk, K. N.; Wu, Y.-D. In *Stereochemistry of Organic and Bioorganic Transformations*; Bartmann, W., Sharpless, K. B., Eds.; VCH Verlagsgesellschaft mbH: Weinheim, 1987; pp 247–260. (d) Wu, Y.-D.; Houk, K. N.; Trost, B. M. *J. Am. Chem. Soc.* **1987**, *109*, 5560. (e) Wu, Y.-D.; Houk, K. N.; Florez, J.; Trost, B. M. *J. Org. Chem.* **1991**, *56*, 3656. (f) Mukherjee, D.; Wu, Y-.D.; Fronczek, F. R.; Houk, K. N. *J. Am. Chem. Soc.* **1988**, *110*, 3328.

(7) SiH_5^- is a known species in the gas phase; see Hajdasz, D. J.; Squires, R. R. *J. Am. Chem. Soc.* **1986**, *108*, 3139.

(8) Frisch, M. J.; Trucks, G. W.; Head-Gordon M.; Gill, P. M. W.; Wong, M. W.; Foresman, J. B.; Johnson, B. G.; Schlegel, H. B.; Robb, M. A.; Replogle, E. S.; Gomperts, R.; Andres, J. L.; Raghavachari, K.; Binkley, J. S.; Gonzalez, C.; Martin, R. L.; Fox, D. J.; Defrees, D. J.; Baker, J.; Stewart, J. J. P.; Pople, J. A. *GAUSSIAN 92*, Revision B; Gaussian, Inc.: Pittsburgh, PA, 1992.

(9) The total energies (–au) calculated with 6-31++G**, MP2/6++G** and MP3/631++G** methods and the zero-point energies (kcal/mol) for the compounds in this reaction are as follows: formaldehyde, 113.874 72, 114.190 59, 114.169 30, 18.2; SiH_5^-, 291.740 03, 291.875 30, 291.899 94, 23.0; CH_3O^-, 114.416 06, 114.770 20, 114.777 27, 23.9; SiH_4, 291.232 03, 291.341 09, 291.362 13, 20.9; **1**, 405.630 23, 406.083 37, 406.114 49, 42.4; **2**, 405.620 04, 406.088 61, 406.115 84, 43.4; **3**, 405.697 27, 406.165 72, 406.195 55, 47.9.

(10) Wu, Y.-D.; Houk, K. N. *J. Am. Chem. Soc.* **1987**, *109*, 906; 2226 and references therein.

(11) Reed, A. E.; Schleyer, P. v. R. *Chem. Phys. Lett.* **1987**, *133*, 553.

0002-7863/93/1515-10992$04.00/0

Table I. Absolute (–au) and Relative Energies (kcal/mol) at Various Levels, Dipole Moments (μ, D), and Cavity Radii (a_0, Å) for SCRF Calculations of the Transition Structures of the Reactions of Cyclohexanone, 1,3-Dioxan-5-one, and 1,3-Dithian-5-one with SiH_5^-

theoretical level[a,b]	parameter	axial TS	equatorial TS	E_{rel}[c]
		Cyclohexanone		
3-21G		596.361 25	596.359 20	1.3
6-31G*		599.633 29	599.629 58	2.3
MP2/6-31G*		600.703 64	600.700 61	**1.9**
6-31G* SCRF		599.635 36	599.633 32	1.3
MP2/6-31G* SCRF		600.696 60	600.695 50	**0.7**
	μ	4.57	4.55	
	a_0	4.37	4.68	
		Dioxanone		
3-21G		667.582 54	667.585 53	–1.9
6-31G*		671.258 56	671.254 38	2.6
MP2/6-31G*		672.407 53	672.410 76	**–2.0**
6-31G* SCRF		671.266 41	671.252 84	8.5
MP2/6-31G* SCRF		672.404 99	672.400 50	**2.8**
	μ	4.40	4.38	
	a_0	5.33	3.45	
		Dithianone		
3-21G		1309.819 21	1309.842 21	–14.4
6-31G*		1316.565 55	1316.574 92	–5.9
MP2/6-31G*		1317.614 05	1317.638 10	**–15.1**
6-31G* SCRF		1316.577 19	1316.574 59	1.6
MP2/6-31G* SCRF		1317.616 40	1317.620 99	**–2.9**
	μ	4.66	4.66	
	a_0	6.06	3.95	

[a] The 6-31G* basis set here is the 6-31G* with a set of diffuse s and p orbitals on the H atoms of SiH_5^-. [b] All energies were calculated on the 3-21G structures. [c] $E_{eq} - E_{ax}$.

are collected in Table I. The MP2/6-31G* results have been found to be consistent with experiment and are used in the following discussion.

In the gas phase, the axial transition structure for the reaction of cyclohexanone is 1.9 kcal/mol more stable than the equatorial one. This gives a 96:4 selectivity, in good agreement with the gas-phase result reported by Ho and Squires.[3] However, the equatorial transition structures for the reactions of dioxanone and dithianone are 2.0 and 15.1 kcal/mol, respectively, more stable than the axial transition structures. These results are similar to those calculated for the reductions with lithium hydride.[1a]

Previously we proposed that these calculated gas-phase stereoselectivities are mainly determined by torsional and electrostatic effects:[1a,b,5,6] The axial addition to cyclohexanone is favored by staggering, which gives minimal torsional strain in the transition structure.[6] This axial preference is even larger for dioxanone due to the shorter ring C–O bonds. Torsional effects favor the equatorial addition to dithianone, because the ring is very puckered due to the long C–S bonds.[1a,6] We also proposed that electrostatic interactions between the nucleophile hydride and the ring heteroatoms strongly disfavor the axial transition structures in the gas phase, resulting in overall equatorial preference for the reaction of dioxanone and an even larger equatorial preference for the reaction of dithianone.[1a] These electrostatic effects may be muted in solution.

The geometries of the transition structures support these arguments. In the axial transition structures of dioxanone and dithianone reactions, the rings are almost in half-chair conformations: the C···H bonds are much longer than those in the equatorial transition structures, and the C–H–Si angles are very bent. These reduce electrostatic interactions in the axial transition structures.

When the solvent effect is included, the axial preference for the cyclohexanone reaction is reduced to 0.7 kcal/mol.[13] The axial transition structure is now 2.8 kcal/mol more stable than the equatorial for the dioxanone reaction, while the equatorial preference for the dithianone is reduced to 2.9 kcal/mol. These calculated stereoselectivities are in agreement with hydride reductions of substituted dioxanones and dithianones by $NaBH_4$ or $LiAlH_4$ or nucleophilic additions by Grignard reagents in solution.[14,15] The solvent reduces unfavorable electrostatic interactions in the axial transition structures,[12] as reflected qualitatively by the calculated dipole moments of these transition structures shown in Table I.

In summary, the transition structures for the hydride reductions of carbonyl compounds by siliconate ion are predicted to involve mainly hydride transfer with no Si–O bonding. The axial reduction is favored for cyclohexanone, while the equatorial reduction is favored for dithianone both in the gas phase and in solution. Reduction of dioxanone is predicted to occur from the equatorial direction in the gas phase due to significant electrostatic destabilization in the axial transition structure but to occur from the axial direction in polar solvents due to large torsional strain in the equatorial transition structure.

Acknowledgment. We are grateful to Professor R. R. Squires of Purdue University for stimulating discussions and for communication of results prior to publication. We are grateful to the National Science Foundation for financial support of this research and to the Center of Computing Services and Telecommunications at The Hong Kong University of Science and Technology and the Pittsburgh Supercomputer Center which supported the calculations.

---

(12) Wong, M. W.; Wiberg, K. B. *J. Chem. Phys.* **1991**, *95*, 8991. Wong, M. W.; Frisch, M. J.; Wiberg, K. B. *J. Am. Chem. Soc.* **1991**, *113*, 4776. Wong, M. W.; Wiberg, K. B.; Frisch, M. J. *J. Am. Chem. Soc.* **1992**, *114*, 523.

(13) For solvent effects in acylic cases, see: Cieplak, A. S.; Wiberg, K. B. *J. Am. Chem. Soc.* **1992**, *114*, 9226.

(14) Boone, J. R.; Ashby, E. C. *Tropics in Stereochemistry*; Eliel, E. I., Allinger, N. L. Eds.; Interscience: New York, 1979; Vol. 11, p 53.

(15) Kobayashi, Y. M.; Lambrecht, J.; Jochims, J. C.; Burkert, U. *Chem. Ber.* **1978**, *111*, 3442. Jochims, J. C.; Kobayashi, Y.; Skrzelewski, E. *Tetrahedron Lett.* **1974**, 571, 575.